JNI 14es Journées Nationales d'Infectiologie

Clermont-Ferrand
et l'interrégion Rhône-Alpes Auvergne

Session de communications orales thématiques : « Infection et dispositif intra-vasculaire »

Le point sur les solutions verrous dans les infections de cathéters veineux centraux longue durée

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Conflits d’intérêts

Subventions pour la recherche
- HEMOTECH
- MSD
- SANOFI
- AVENTIS
- DGOS (PHRC)

Consultant
- BAYER SANTE

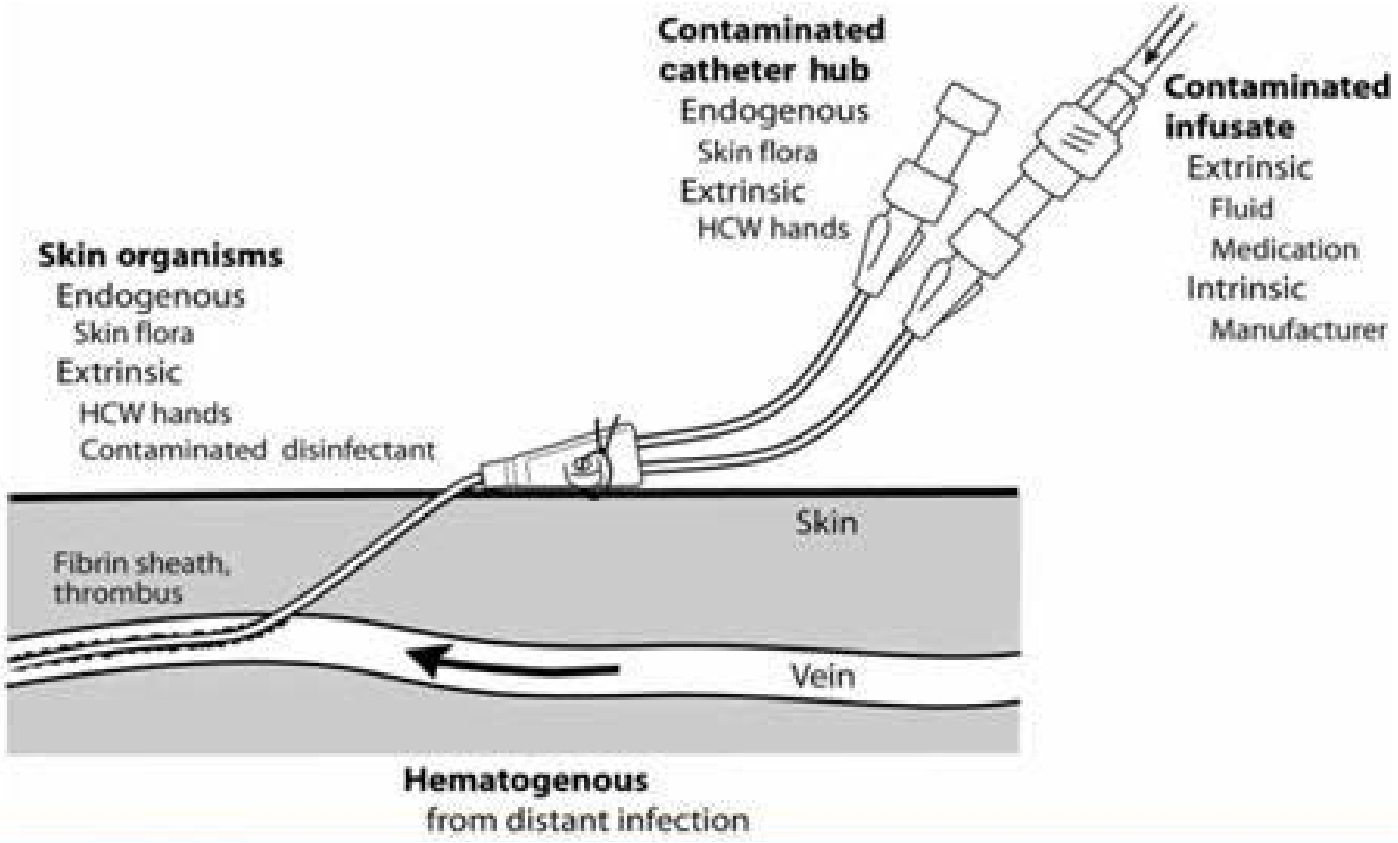
Salarié
- Ministère de l’Enseignement Supérieur et de la Santé

Objectifs de la présentation :

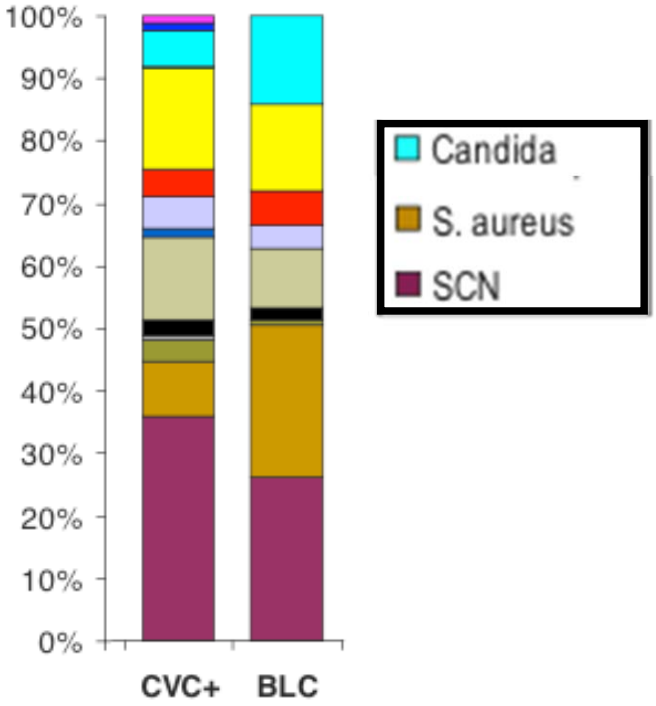
- Connaître la nature et les conditions d'utilisation des solutions verrous en préventif et curatif

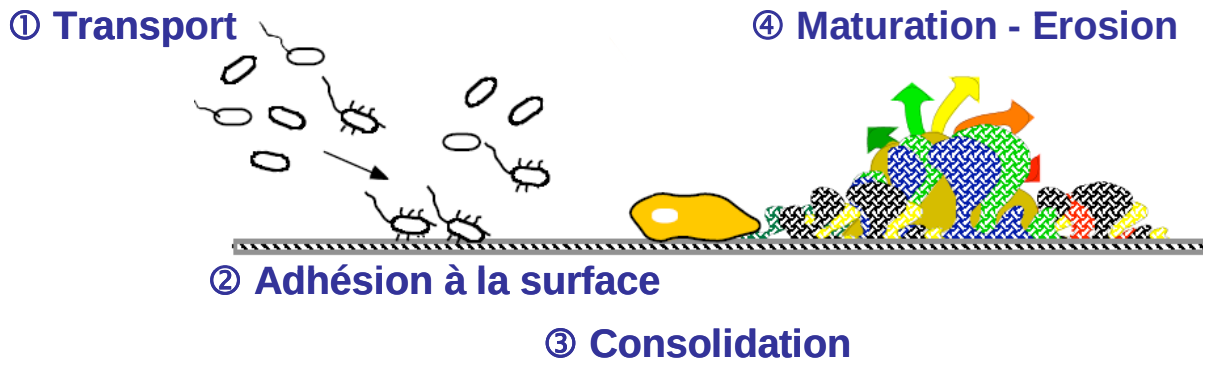
- Connaître l'efficacité des solutions verrous en préventif et curatif selon le type de cathéter central utilisé

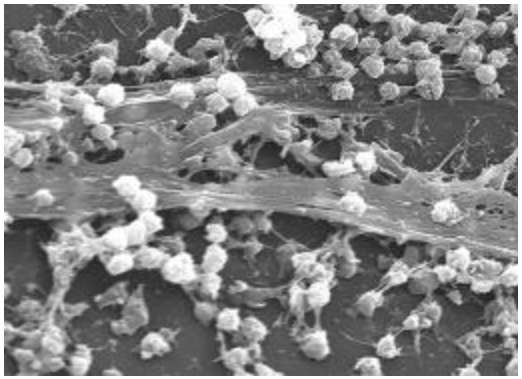
Mechanisms of Catheter Colonization

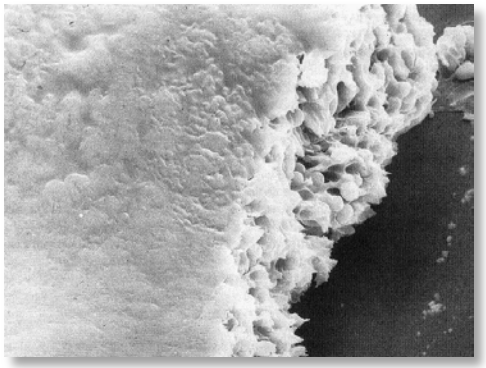


- Voie endoluminale
  - Manipulation lignes et cathéters +++
  - Infusats contaminés


100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
CVC+
BLC
Candida
S. aureus
SCN


① Transport
④ Maturation - Erosion
② Adhésion à la surface
③ Consolidation





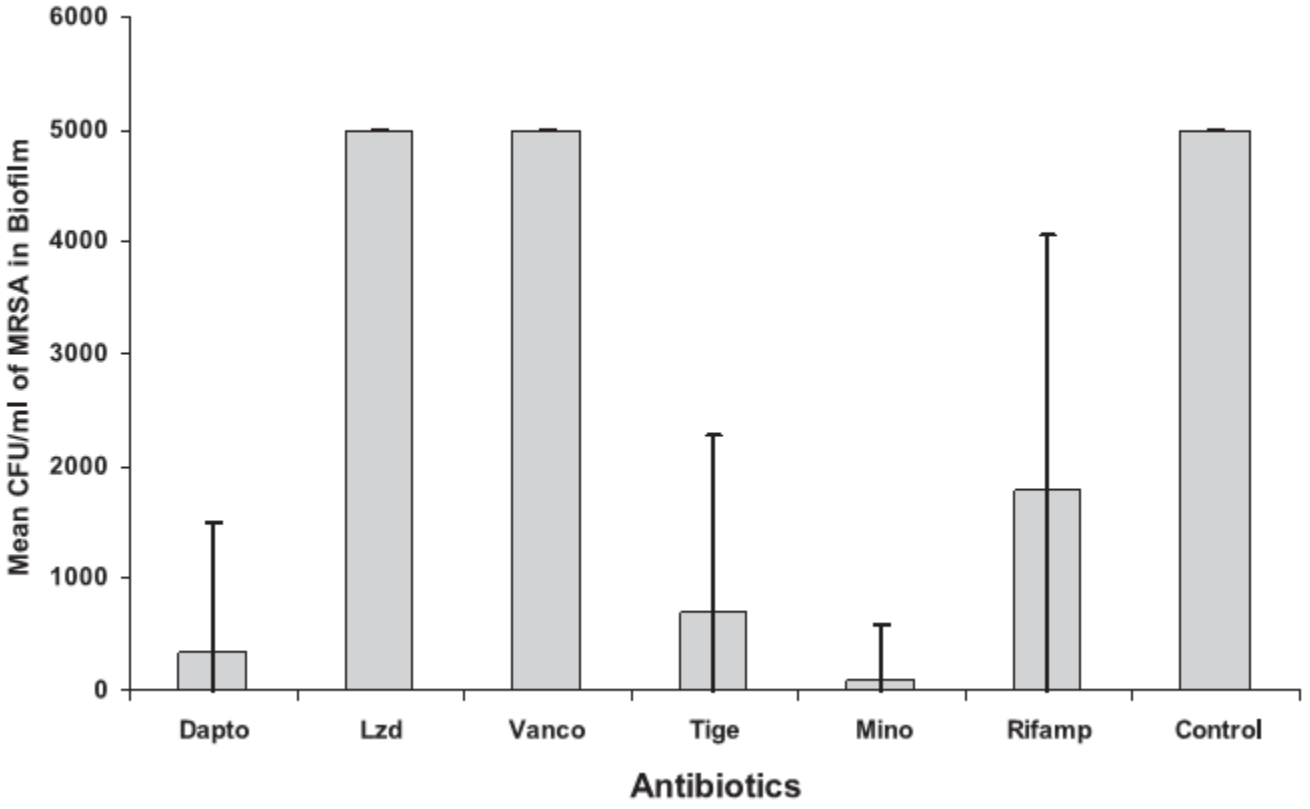
Susceptibility of biofilm organisms

Organism	Antibiotic	MIC or MBC (mcg/mL)	Effective [ ] vs. biofilm (mcg/mL)
S. aureus (NCTC 8325-4)	Vancomycin	2 (MBC)	20
P. aeruginosa (ATCC 27853)	Imipenem	1 (MIC)	>1,024[a]
E. coli (ATCC 25922)	Ampicillin	2 (MIC)	512[a]
P. pseudomallei	Ceftazidime	8 (MBC)	800
S. sanguis	Doxycycline	0.063 (MIC)	3.15

[a] Minimal biofilm eradication

Adapted from Donlan RM, et al. *Clin Microbiol Rev*. 2002;15:167-93.

Activities of antibiotics against MRSA bacteria embedded in biofilm after 24 h of exposure



Raad I, Antimicrob Agents Chemother. 2007

Technique du verrou anti-infectieux :

- Instillation d'une solution antimicrobienne

- Concentration élevée sur le site

- Durée

- Stratégie
  - Préventive
  - Curative « catheter salvage »

- Efficacité limitée à la surface endoluminale

Solutions verrous :

- Antibiotiques
    - glycopeptides, aminosides, céphalosporines, pénèmes, lipopeptide, oxazolidinone, cylines

- Biocides
    - citrates, taurolidine, bleu de méthylène, parabènes, NAC, HCl, éthanol…

- Anticoagulants / fibrinolytiques: héparine, citrate, EDTA, r-tPA

- Multiple combinaisons
  antimicrobiens
  +/- anticoagulants

Solutions verrous :

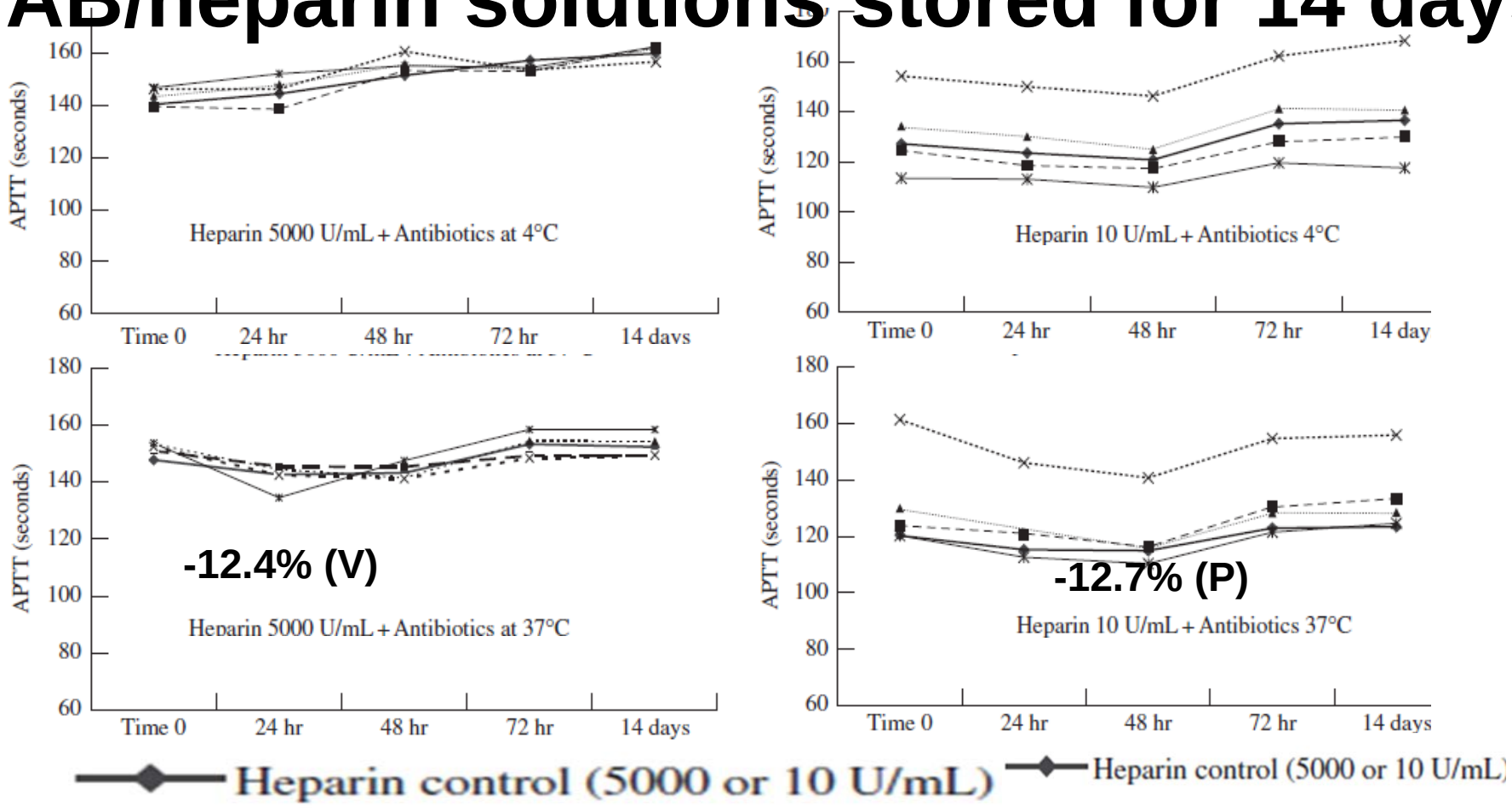
- Stabilité chimique solutions verrous
    - Type et concentrations des composants
    - Type d’ élastomères
    - Efficacité antibiofilm/anticoagulante

- Biocompatibilité, interactions contenu/contenant bidirectionnelles
    - Types d’élastomères
    - Dégradation de l’ élastomères (silicone / PU)
    - Rupture, dysfonction, thrombose

-Dispositifs médicaux IIB ou III ; diffusion systémique/rétrograde
    - Toxicité

- Ecologie (résistance ?) au sein du biofilm et à distance

Biological activity of heparin in AB/heparin solutions stored for 14 days



The largest drops in APTT from baseline were <13% and only transiently observed

These variations are unlikely to be of clinical relevance

Adapted from Robinson JL, *J Antimicrobial Chemother* 2005

Antibiotic-Heparin Lock: In Vitro Antibiotic Stability Combined with Heparin in a Central Venous Catheter

	Vancomycin 10 mg/ml and Heparin 5000 U/ml (6 catheters)				
Hours	Absorbance (mean ± SD)	%[a]	p Value[b]	%[e]	p Value[f]
0	0.936 ± 0.003				
48	0.691 ± 0.007	-26.2	<0.001	-22.0	<0.0001
72	0.658 ± 0.012	-29.7	<0.001	-27.2	<0.0001

d' après Vercaigne LM, *Pharmacotherapy* 2000

In vitro stability of vancomycin mixed with 4% citrate

Storage temperature	37 °C	37 °C	37 °C	37 °C
Solution	4% citrate	4% citrate	4% citrate	4% citrate
Container	Hemostar catheter	Hemostar catheter	CardioMed catheter	CardioMed catheter
Nominal concentration (mg/mL)	1	3	1	3
Initial concentration (mg/mL)	1.19 ± 0.00	2.81 ± 0.00	1.04 ± 0.00	2.63 ± 0.00
Study day				
1	92.243	96.594	99.669	102.537
3	98.076	95.297	102.669	104.857
Time to achieve a 10% change in concentration (days)[b]	52.2	6.4	9.7	6.7

On day 3, >92% of the initial vancomycin concentration remained in all containers at both concentrations

Battistella M, Hemo Int 2009

In vitro stability of gentamicin mixed with 4% citrate

Table: Percent remaining during storage

Hour	Gentamicin 2.5mg/mL	Sodium citrate 40 mg/mL
0	99.36+/-1.24	100.8+/-0.95
24	104.8+/-3.32	102.6+/-1.55
48	101.6+/-0.62	102.7+/-1.71
72	103.4+/-0.67	104.1+/-1.07
96	102.4+/-1.03	102.9+/-1.25
	P=0.2769	P=0.5556

The stability of the mixture was assessed by the concentrations of gentamicin and sodium citrate determined by HPLC assays

Adapted from Battistella M, *Hemo Int* 2010

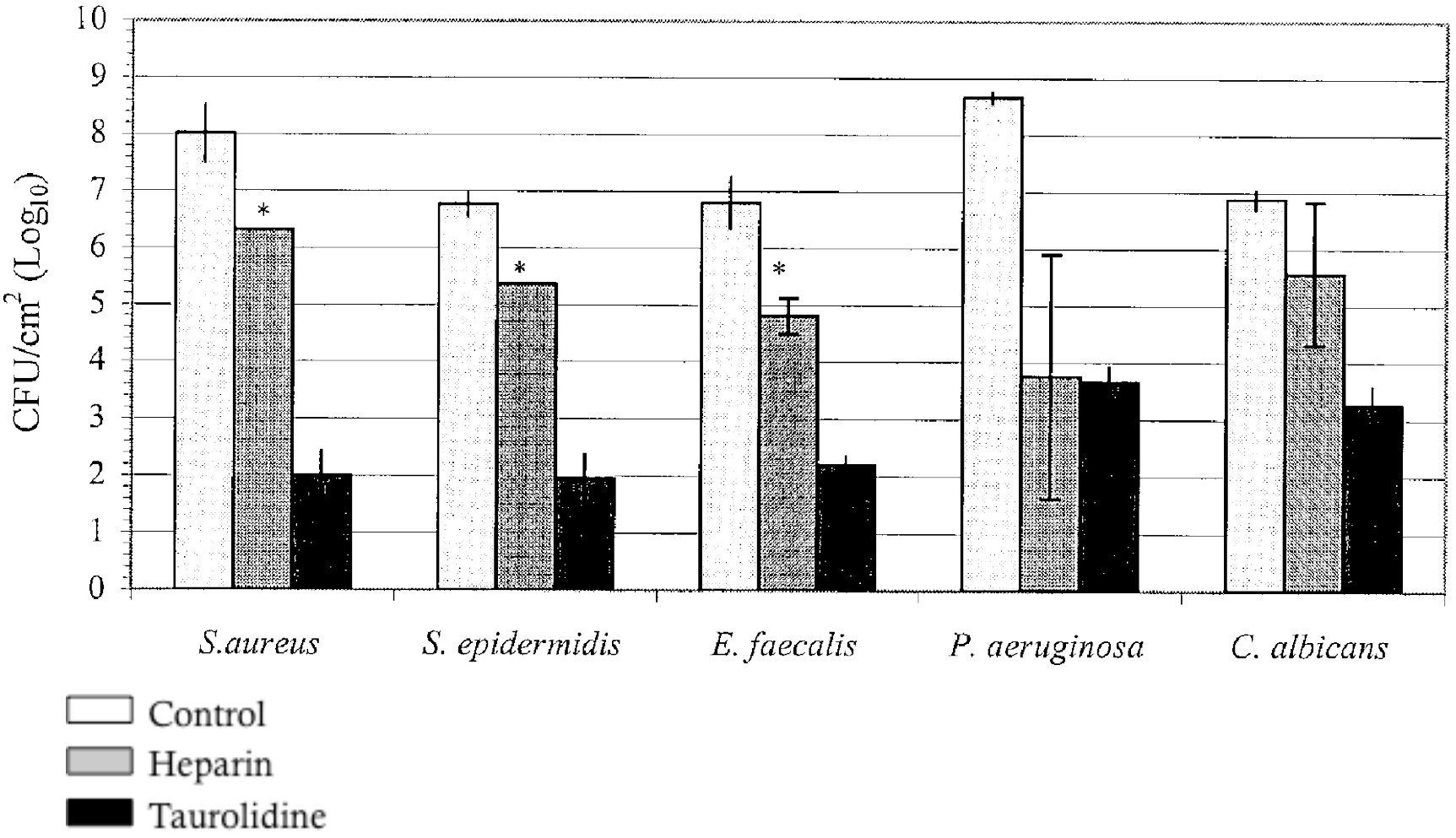
Final concentrations of antibiotic lock solutions used for the treatment of catheter-related bloodstream infection.

Antibiotic and dosage	Heparin or saline, IU/mL
Vancomycin, 2.5 mg/mL	2500 or 5000
Vancomycin, 2.0 mg/mL	10
Vancomycin, 5.0 mg/mL[a]	0 or 5000
Ceftazidime, 0.5 mg/mL	100
Cefazolin, 5.0 mg/mL	2500 or 5000
Ciprofloxacin, 0.2 mg/mL[b]	5000
Gentamicin, 1.0 mg/mL	2500
Ampicillin, 10.0 mg/mL	10 or 5000
Ethanol, 70%[c]	0

A precipitate appears when mixing heparin with antimicrobial agents

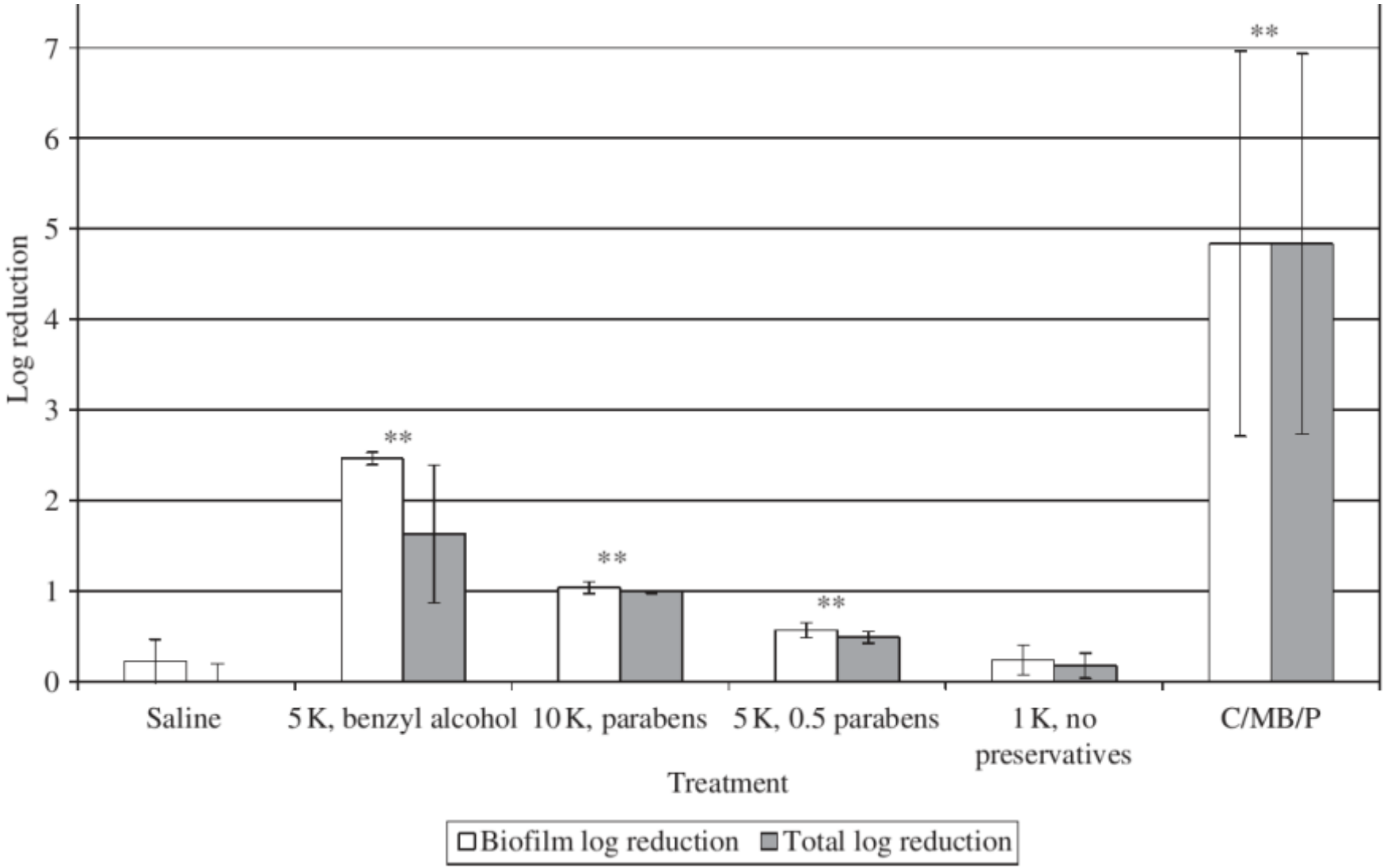
Mermel L, IDSA guidelines, CID 2009

Comparison of the efficacies of taurolidine-citrate and heparin against biofilm organisms

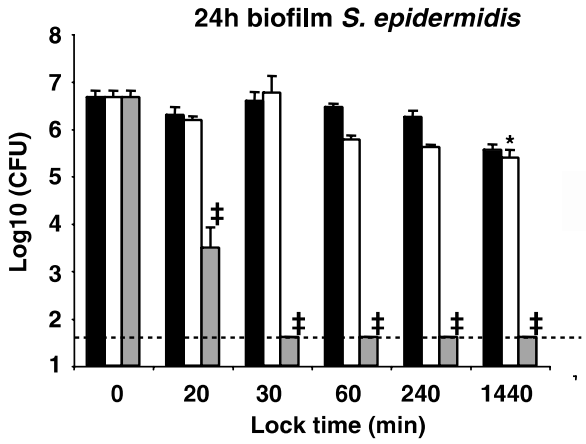


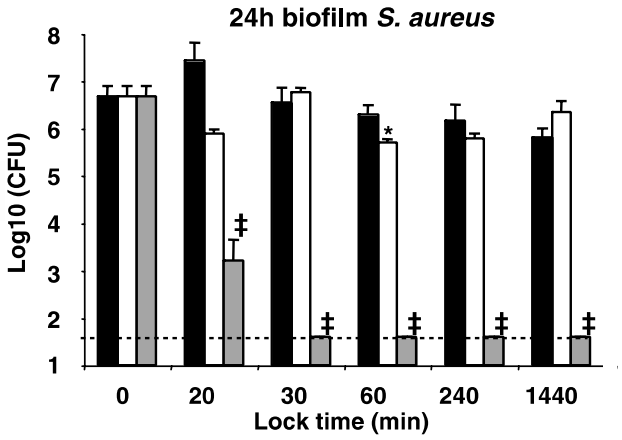
Shah CB, Antimicrob Agents Chemother. 2002

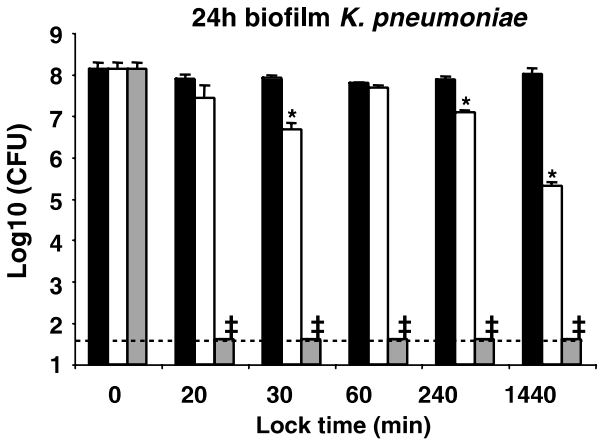
Susceptibility of S. aureus biofilms to various tested solutions (heparins, C/MB/P) following 48 h of treatment under static conditions. Log reduction for flow cell-grown biofilms (white bars) and for flow cell-grown biofilms plus *S. Aureus* cells present in the bulk liquid (grey bars) was determined by viability counts. **P,0.01.

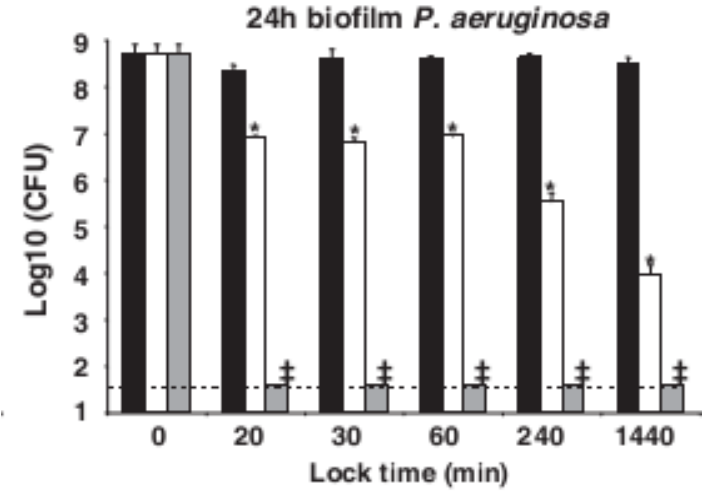


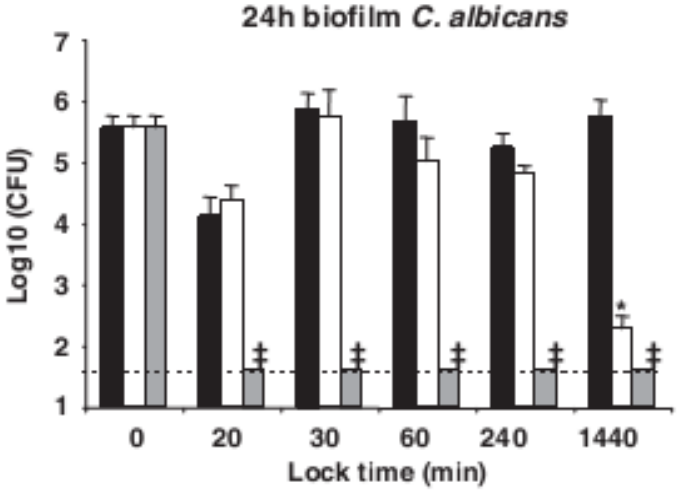
Sauer K, J Antimicrob Chemother 2009

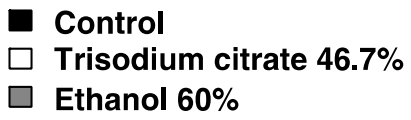






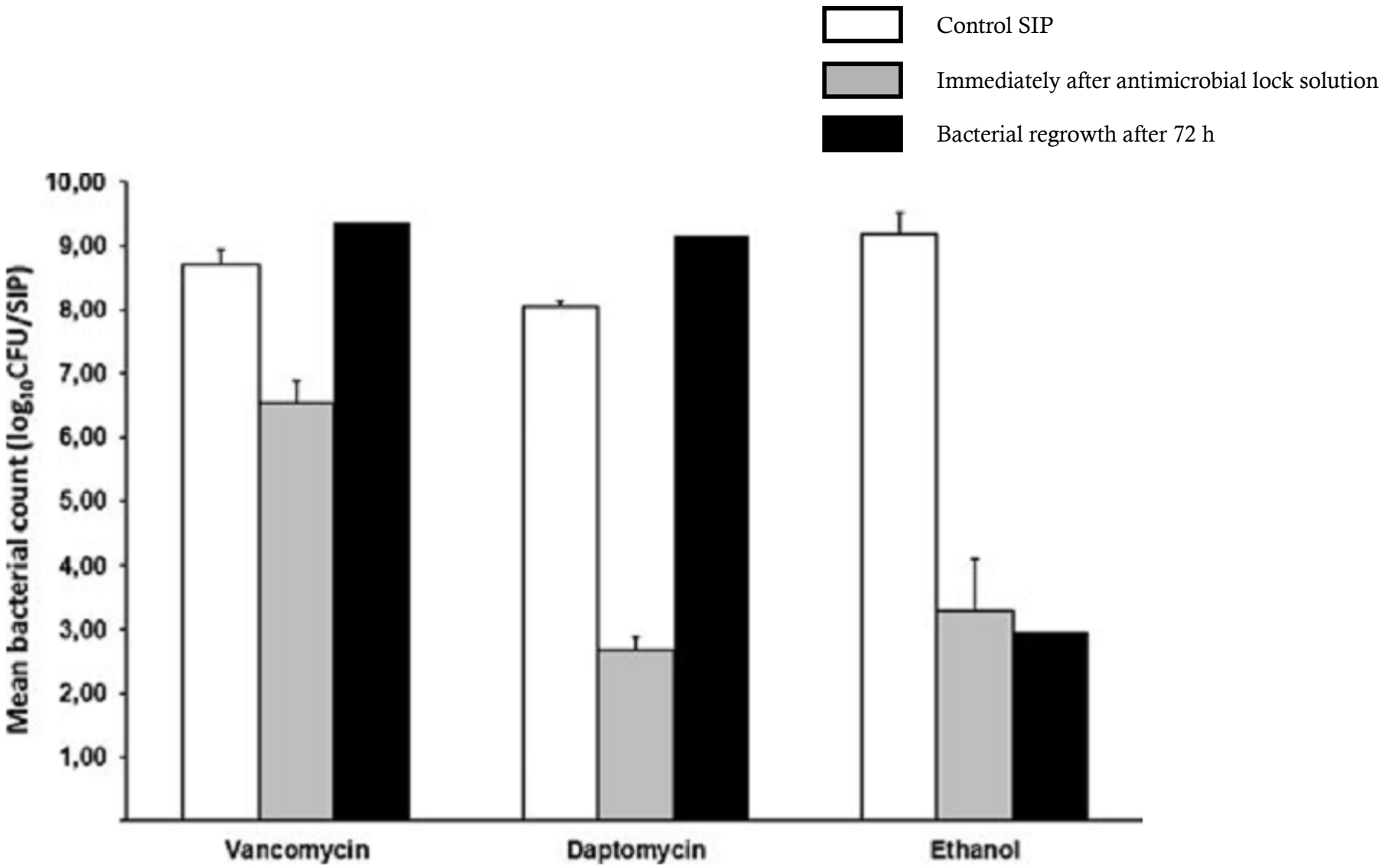






Balestrino D, Nephrol Dial Transplant 2009

Mean bacterial count in control SIP immediately after AML solution and bacterial revival after 24 h of exposure to antimicrobial LS followed by 72 h in the biofilm development system.



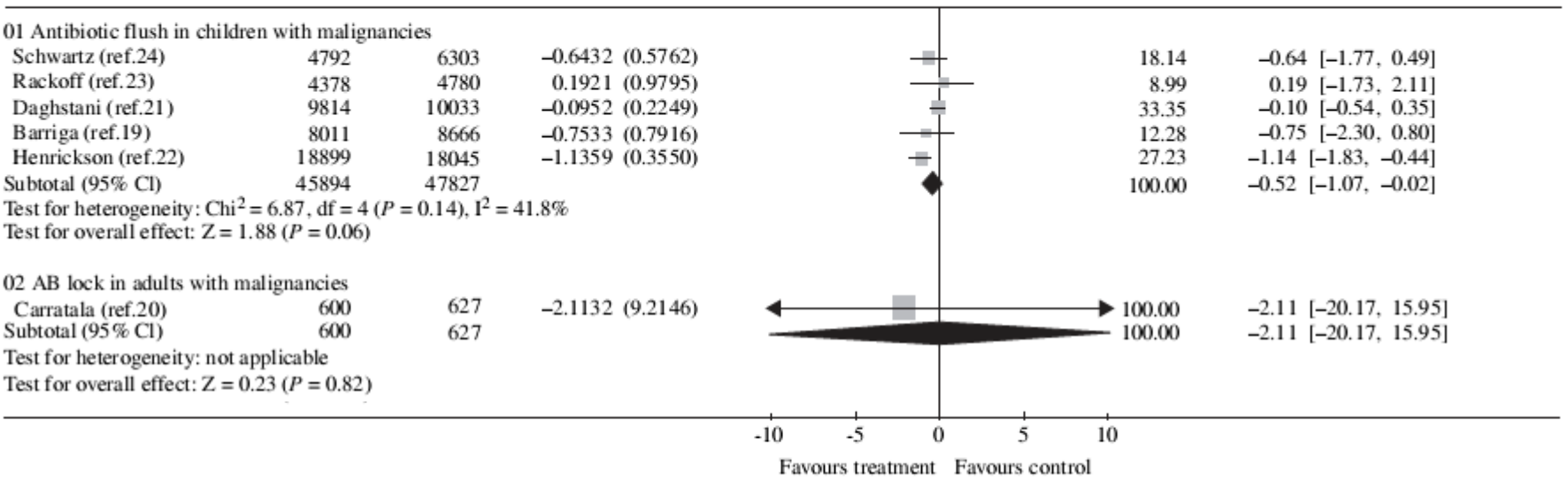
Aumeran C, Eur J Clin Microbiol Infect Dis 2013

Antimicrobial lock for preventing CRBSI

In trials studying oncology patients the estimated effect showed only a marginal significant benefit in favour of antibiotic-based lock solutions

Review: Use of antibiotic-based lock solutions to prevent catheter-related bloodstream infection. A systematic review of randomized controlled trials.
Comparison: 03 Antibiotic-based lock solutions versus heparin lock solution in oncology patients
Outcome: 02 Incidence density difference of BSI per 1000 catheter days

Study or sub-category	Treatment N	Control N	IDD (SE)	Weight %	IDD (random) 95% CI
01 Antibiotic flush in children with malignancies					
Schwartz (ref.24)	4792	6303	−0.6432 (0.5762)	18.14	−0.64 [−1.77, 0.49]
Rackoff (ref.23)	4378	4780	0.1921 (0.9795)	8.99	0.19 [−1.73, 2.11]
Daghstani (ref.21)	9814	10033	−0.0952 (0.2249)	33.35	−0.10 [−0.54, 0.35]
Barriga (ref.19)	8011	8666	−0.7533 (0.7916)	12.28	−0.75 [−2.30, 0.80]
Henrickson (ref.22)	18899	18045	−1.1359 (0.3550)	27.23	−1.14 [−1.83, −0.44]
Subtotal (95% CI)	45894	47827		100.00	−0.52 [−1.07, −0.02]
Test for heterogeneity: $Chi^2 = 6.87$, df = 4 ($P = 0.14$), $I^2 = 41.8\%$					
Test for overall effect: Z = 1.88 ($P = 0.06$)					
02 AB lock in adults with malignancies					
Carratala (ref.20)	600	627	−2.1132 (9.2146)	100.00	−2.11 [−20.17, 15.95]
Subtotal (95% CI)	600	627		100.00	−2.11 [−20.17, 15.95]
Test for heterogeneity: not applicable					
Test for overall effect: Z = 0.23 ($P = 0.82$)					



In the oncology patients NNT was 8 to prevent one BSI, given a mean insertion time of 227 days (range: 154–295) and average baseline risk of 1.7 events per 1000 catheter-days

Snaterse M, J Hosp Infect 2010

Central Venous Catheter Care for the Patient With Cancer: American Society of Clinical Oncology Clinical Practice Guideline

2. What is effective prophylaxis for the prevention of catheter-related infections

2.4. There are conflicting data about the relative value of prophylactic heparin with saline flushes to prevent catheter-associated bloodstream infections or thrombosis; data are not sufficient to recommend for or against routine use of antibiotic-flush/antibiotic-lock therapy

Schiffer CA, J Clin Oncol 2013

Randomized controlled trial of taurolidine citrate versus heparin as catheter lock solution in paediatric patients with haematological malignancies

Table III
Infections and complications in patient groups

	Group 1 (heparin)	Group 2 (TauroLock™)	*P*-value
No. of patients	36	35	
Clinical infections (FUOs)	25 (69%)	22 (63%)	NS
Time until first infection after start of locking (days)	41.2 ± 49.4	35.6 ± 31.8	NS
Use of intravenous antibiotics (days)	25.3 ± 25	18.1 ± 24.7	NS
Clinical infections per 1000 catheter-days	9.5 ± 10	10.3 ± 11.6	0.916
Clinical infections per 1000 locking-days	9.9 ± 10.3	10.7 ± 11.8	0.981
BSI			
Patients without BSI	27	33	0.032
With BSI	9	2	
No. of BSIs per 1000 catheter-days	1.3 ± 2.5	0.3 ± 1.2	0.03[a]
No. of BSIs per 1000 locking-days	1.3 ± 2.6	0.3 ± 1.3	0.03[a]

FUO, fever of unexplained origin; BSI, bloodstream infection; NS, non-significant.
[a] Mann–Whitney *U*-test.

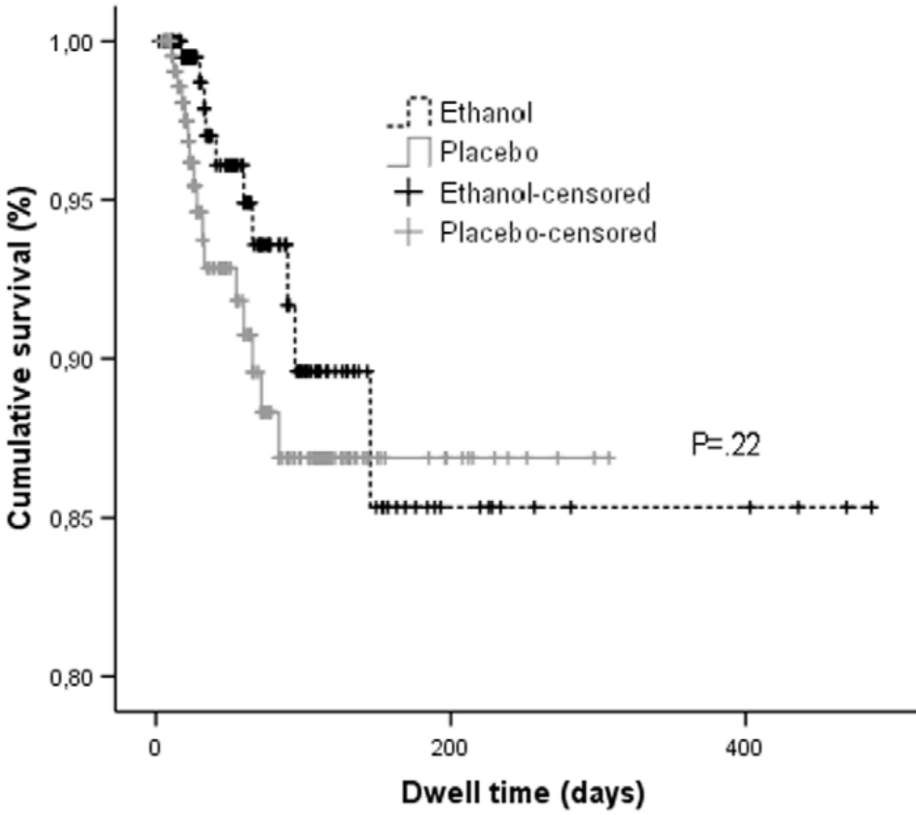
In a multivariate logistic regression model, time without lock but not the type of lock solution was the only significant predictor of overall catheter colonization (P=0.004).

Dümichen M J, J Hosp Infection 2011

Ethanol Lock against CRBSI in adult hematology patients

Table 2. Overview of endpoints and other parameters.

Parameter	Ethanol (n = 226)	Placebo (n = 222)	P
Strictly endoluminal CRBSI	2	7	.10
Presumed endoluminal CRBSI	8	9	.81
Combined primary endpoint	10	16	.23
Primary bacteremia	91	91	.95
Positive culture of catheter hub[a]	8	11	.67
Positive culture of catheter tip[b]	49	57	.52
Exoluminal CRBSI	11	8	.64



3 mL of 70% ethanol solution was locked for 15 minutes per day

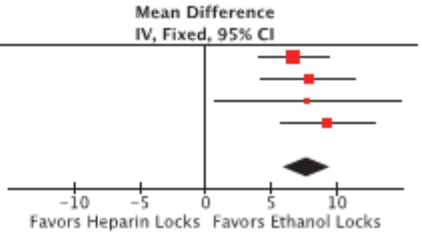
Slobbe S, PloS One 2010

All studies were pre /post studies

(a) Pooled mean difference of CRBSI rate

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Fixed, 95% CI
Cober 2010	6.7	1.38	44.3%	6.70 [4.00, 9.40]
Jones 2010	7.8	1.83	25.2%	7.80 [4.21, 11.39]
Mouw 2008	7.76	3.62	6.4%	7.76 [0.66, 14.86]
Wales 2011	9.3	1.87	24.1%	9.30 [5.63, 12.97]
Total (95% CI)			**100.0%**	**7.67 [5.87, 9.47]**

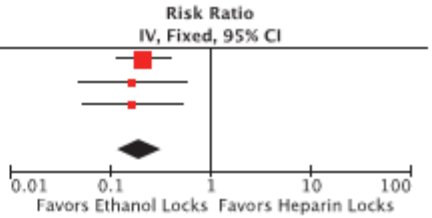
Heterogeneity: $\chi^2 = 1.26$, df = 3 ($P = .74$); $I^2 = 0\%$
Test for overall effect: Z = 8.36 ($P < .00001$)



(b) Pooled relative risk of CRBSI rate

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
Jones 2010	−1.55	0.33	63.3%	0.21 [0.11, 0.41]
Mouw 2008	−1.81	0.64	16.8%	0.16 [0.05, 0.57]
Wales 2011	−1.81	0.59	19.8%	0.16 [0.05, 0.52]
Total (95% CI)			**100.0%**	**0.19 [0.12, 0.32]**

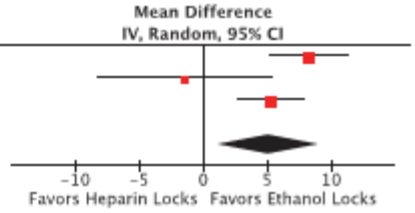
Heterogeneity: $\chi^2 = 0.23$, df = 2 ($P = .89$); $I^2 = 0\%$
Test for overall effect: Z = 6.26 ($P < .00001$)



(c) Pooled mean difference of catheter replacements

Study or Subgroup	Mean Difference	SE	Weight	Mean Difference IV, Random, 95% CI
Jones 2010	8.2	1.59	38.6%	8.20 [5.08, 11.32]
Mouw 2008	−1.46	3.53	19.9%	−1.46 [−8.38, 5.46]
Wales 2011	5.3	1.33	41.6%	5.30 [2.69, 7.91]
Total (95% CI)			**100.0%**	**5.07 [1.12, 9.03]**

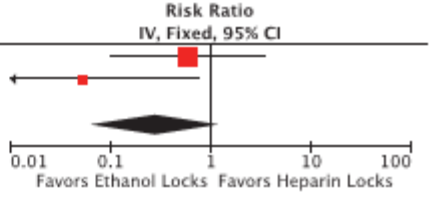
Heterogeneity: $\tau^2 = 8.04$; $\chi^2 = 6.64$, df = 2 ($P = .04$); $I^2 = 70\%$
Test for overall effect: Z = 2.51 ($P = .01$)



(d) Pooled relative risk of catheter replacements

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
Mouw 2008	−0.53	0.91	69.1%	0.59 [0.10, 3.50]
Wales 2011	−2.93	1.36	30.9%	0.05 [0.00, 0.77]
Total (95% CI)			**100.0%**	**0.28 [0.06, 1.23]**

Heterogeneity: $\chi^2 = 2.15$, df = 1 ($P = .14$); $I^2 = 54\%$
Test for overall effect: Z = 1.68 ($P = .09$)



Oliveira C, Pediatrics 2012

Preventive antimicrobial catheter locks in chronic hemodialysis patients

Table 3 | Published meta-analyses on the use of antibiotic lock solutions in patients on hemodialysis

Study	Randomized, controlled trials (*n*)	Patients (*n*)	Risk ratio of bacteremia (95% CI)*
James *et al.* (2008)[39]	11	765	0.32 (0.22–0.47)
Yahav *et al.* (2008)[40]	11	924	0.44 (0.38–0.50)
Jaffer *et al.* (2008)[41]	7	624	0.13 (0.10–0.20)
Labriola *et al.* (2008)[42]	8	829	0.32 (0.10–0.42)

*The presence of catheter-related bloodstream infection, as a dichotomous outcome.

The use of intraluminal antimicrobial lock solutions reduces the rate of CVC-related bacteremia by 56–87%

Antibiotics that have been used alone or in combination for lock solutions include vancomycin, gentamicin, ciprofloxacin, minocycline, amikacin, cefazolin, cefotaxime, and ceftazidime.

Li, P. K. Nat. Rev. Nephrol. 2011

Preventive antimicrobial catheter locks in chronic hemodialysis patients, recent RCTs

Trial, year	N° .of patients	CLABSI rate, cases/ 1,000 CDs: Control group	CLABSI rate, cases/ 1,000 CDs: ALS Group	*P*	ALS constituents
Power et al, 2009	232	0.7	0.8	> 0.05	46.7% citrate
Solomon et al, 2010	110	2.4	1.4	.1	Taurolidine-citrate
Campos et al, 2011	150	4.3	1.1	0.005	Minocycline-EDTA
Hemmelgarn et al, 2011	225	1.37	0.4	0.02	rtPA-heparin
Maki et al, 2011	407	0.82	0.24	0.005	C-MB-P
Moran et al, 2012	303	0.91	0.28	0.003	Gentamicin-citrate
Broom et al, 2012	49	3	1	0.12	70% Ethanol

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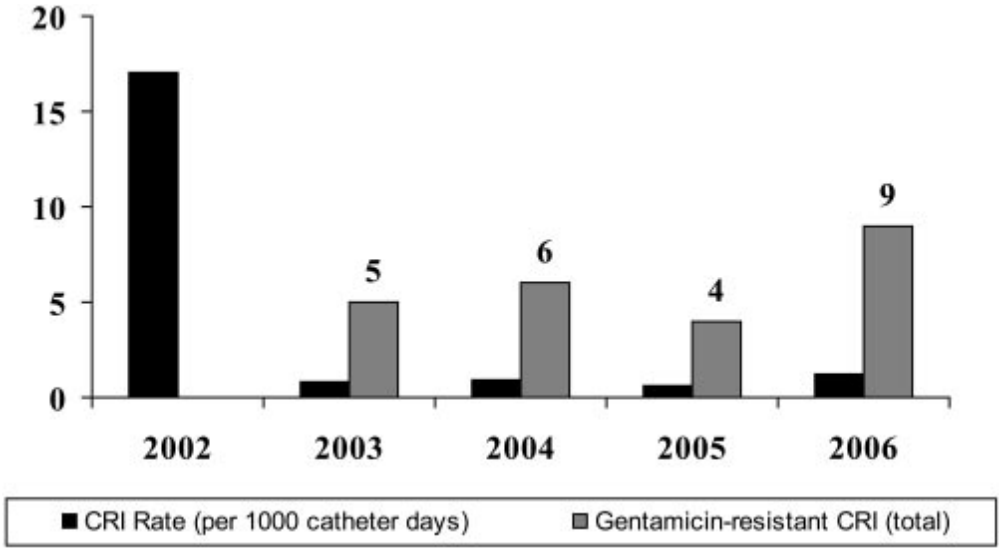
Antimicrobial Lock Solutions
emergence of resistance to the antimicrobial agent used

Gentamicin and heparin lock (GHL) protocol in 1410 chronic hemodialysis patients



CRBSI rates and cases of gentamicin resistance

Table 4. Characteristics of gentamicin-resistant bacteremias

Patient Characteristics	n = 24 (%)
Duration of GHL (days; mean)	297.5
Prior parenteral aminoglycoside exposure	4 (17)
Gentamicin-resistant pathogen	
Coagulase-negative staph	13 (54)
Enterococcus faecalis	7 (29)
Streptococcus species	2 (8)
Methicillin-resistant *Staphylococcus aureus*	1 (4)
Brevibacterium species	1 (4)
Complications	
Catheter removed	12 (50)
Endovascular infection[a]	5 (21)
Sepsis	4 (17)
Hospital admission	10 (42)
Intensive care unit admission	2 (8)
Death within 60 days	4 (17)
Length of hospital stay (days; mean)	9.7

[a]Four cases of subacute bacterial endocarditis and one case of aortic arch thrombus.

Landry DL, Clin J Am Soc Nephrol 2010

Anti-microbial locks increase the prevalence of Staphylococcus aureus and antibiotic-resistant Enterobacter

	Gentamicin resistance, RR (95% CI)	P	Ciprofloxacin resistance, RR (95% CI)	P
All Gram-negative cultures	1.57 (0.95–2.62)	0.07	1.18 (0.79–1.77)	0.42
Enterobacter species	Infinity[a]	< 0.0001	6.00 (1.41–25.47)	0.01
Pseudomonas species	0.78 (0.40–1.52)	0.46	0.99 (0.53–1.83)	0.90
Escherichia coli species	0.97 (0.26–3.58)	0.90	2.03 (0.47–8.75)	0.34

[a]No gentamicin-resistant *Enterobacter* was isolated in the control group, hence the value of infinity. This is clearly an impossible situation. If a single case had been found, then the RR would equal 15.29. We can therefore assume that the RR is > 15.29. Figures in parentheses are 95% confidence intervals. NA, not applicable.

In addition to the systemic antibiotics, the study group (n = 662) received AML containing vancomycin and gentamicin during inter-dialytic periods.

Dixon JJ, Nephrol Dial Transplant 2012

Preventive antimicrobial catheter locks in chronic hemodialysis patients, recent RCTs

Trial, year	N° .of patients	CLABSI rate, cases/ 1,000 CDs: Control group	CLABSI rate, cases/ 1,000 CDs: ALS Group	*P*	ALS constituents
Power et al, 2009	232	0.7	0.8	> 0.05	46.7% citrate
Solomon et al, 2010	110	2.4	1.4	.1	Taurolidine-citrate
Campos et al, 2011	150	4.3	1.1	0.005	Minocycline-EDTA
Hemmelgarn et al, 2011	225	1.37	0.4	0.02	rtPA-heparin
Maki et al, 2011	407	0.82	0.24	0.005	C-MB-P
Moran et al, 2012	303	0.91	0.28	0.003	Gentamicin-citrate
Broom et al, 2012	49	3	1	0.12	70% Ethanol

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Power et al, 2009	232	0.7	0.8	> 0.05	4.3 vs 8, P<0.001	46.7% citrate
Solomon et al, 2010	110	2.4	1.4	.1	HR = 0.4, p=0.008	Taurolidine-citrate
Campos et al, 2011	150	4.3	1.1	0.005	3.2 vs 4.6, P=0.31	Minocycline-EDTA
Hemmelgarn et al, 2011	225	1.37	0.4	0.02	HR = 1.91, p=0.02	rtPA-heparin
Maki et al, 2011	407	0.82	0.24	0.005	4 vs 0, P=0.04	C-MB-P
Moran et al, 2012	303	0.91	0.28	0.003	2.4 vs 3.4, P=0.2	Gentamicin-citrate
Broom et al, 2012	49	3	1	0.12	1.6 vs 1.4, P=0.82	70% Ethanol

Embolic Complications From Central Venous Hemodialysis Catheters Used With Hypertonic Citrate Locking Solution

Table 1. Characteristics of Patients With Catheter Emboli

Patient No.	Age (y)	Sex	Catheter Position	Duration (mo)	Anticoagulant	Hypotension	Embolus
1	32	F	Right subclavian catheter	24	Tinzaparin 1,500 IU	No	Cerebrovascular accident
2	79	M	Left internal jugular central venous catheter	4	Daily tinzaparin	Yes	Pulmonary embolus
3	64	F	Right internal jugular central venous catheter	3	Tinzaparin 3,500 IU	Yes	Pulmonary embolus
4	86	M	Left internal jugular central venous catheter	6	Tinzaparin 2,500 IU	Yes	Pulmonary embolus
5	68	F	Right internal jugular central venous catheter	5	Tinzaparin 2,500 IU	Yes	Pulmonary embolus
6	30	M	Right internal jugular central venous catheter	3	Warfarin	Yes	Pulmonary embolus
7	23	F	Right internal jugular central venous catheter	1	Tinzaparin 1,500 IU	Yes	Pulmonary embolus
8	56	M	Right internal jugular central venous catheter	3	Tinzaparin 4,500 IU	No	Pulmonary embolus

Note: Duration refers to the time since the central venous catheter was inserted; hypotension refers to hypotension shortly after starting dialysis; and type of embolus is categorized as pertaining to brain (cerebrovascular accident) or lung (pulmonary embolus).

Willicombe MK, Am J Kidney Dis 2010

Nephrol Dial Transplant (2012) 27: 2953–2957
doi: 10.1093/ndt/gfs048
Advance Access publication 30 March 2012

Trisodium citrate induced protein precipitation in haemodialysis catheters might cause pulmonary embolism

Gernot Schilcher[1], Hubert Scharnagl[2], Joerg H. Horina[1], Werner Ribitsch[1], Alexander R. Rosenkranz[1], Tatjana Stojakovic[2] and Hans-Dietrich Polaschegg[1,3]

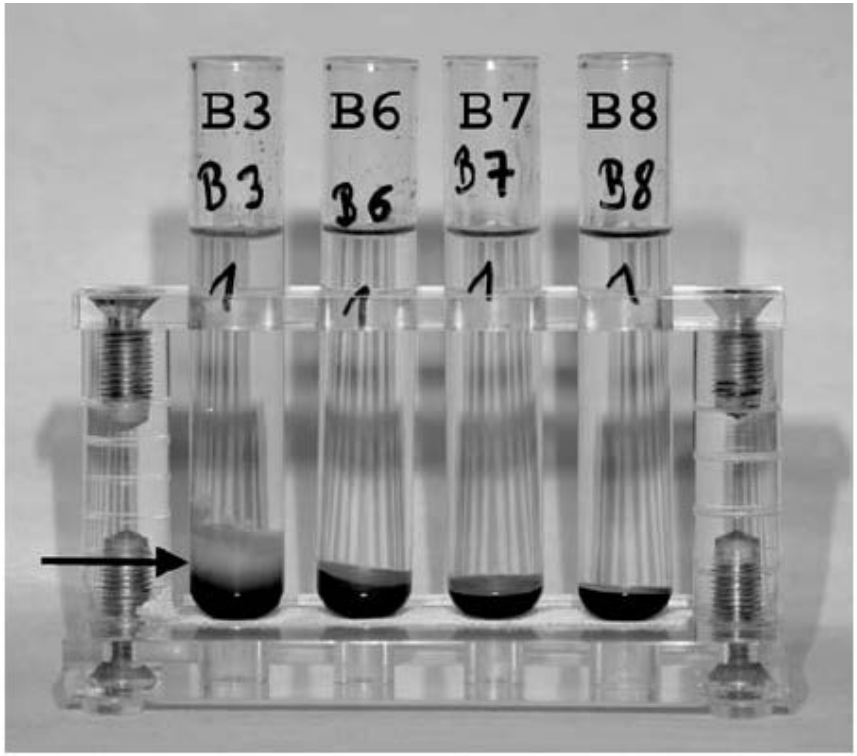


Fig. 1. The arrow indicates the precipitated protein within the test tube (B3) after centrifugation of the test solution consisting of 1 mL WB and 4 mL citrate 32.7%. The tubes with test solutions containing citrate of <12% in the dilution series (B6 with 11.7%; B7 with 9.3% and B8 with 4.7%) revealed no signs of protein precipitation.

Antibiotic Lock Prophylaxis, Antimicrobial Catheter Flush and Catheter Lock Prophylaxis

Use prophylactic antimicrobial lock solution in patients with long term catheters who have a history of multiple CRBSI despite optimal maximal adherence to aseptic technique. Category II

IDSA guidelines, O'Grady CID 2011

In view of the potential risks of spillover of the locking solution, associated risks (arrhythmias, toxicity, allergic reactions, development of resistance to antibiotics, catheter dysfunctions) should be balanced with the benefits in terms of prevention of infection.

Complementary studies with biocide are mandatory for recommending systematic antimicrobial lock prophylaxis

Personnal opinion

Antimicrobial lock for treating CRBSI

Treatment of Catheter infections

Catheter removal is the first therapeutic option
in case of

- Catheter no longer needed
- Hemodynamically unstable patients
- Metastatic infections
  Endocarditis, thrombophlebitis, osteomyelitis
- Infections with *S. aureus* , *P. aeruginosa,* fung*i*
- Infection with multi-resistant organisms
- Tunnel infection with fever

In combination with systemic ABs

Vanholder R, NDT Plus 2010; 3: 234–246

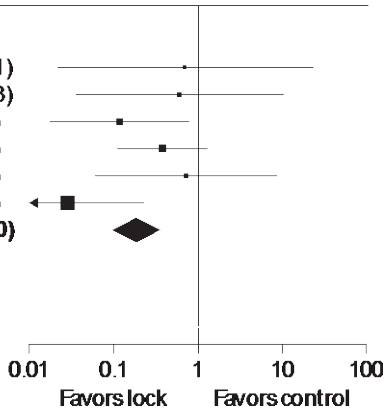
Catheter salvage without antimicrobial lock is associated with a high(er) rate of treatment failure and of recurrent bacteremia

Incidence of catheter replacement

Study or subgroup	Lock events	Lock total	Systemic antibiotics events	Systemic antibiotics total	Weight %	OR M-H, fixed (95% CI)
1.1.2 Lock + systemic antibiotics						
Messing et al. [16], 1988	1	11	0	2	1.7	0.71 (0.02, 23.31)
Dannenberg et al. [10], 2003	1	24	1	15	2.8	0.61 (0.04, 10.53)
Lee et al. [12], 2005	2	16	6	11	15.0	0.12 (0.02, 0.79)
Rijnders et al. [15], 2005	7	21	13	23	19.9	0.38 (0.11, 1.31)
Fortun et al. [11], 2006	1	19	2	29	3.6	0.75 (0.06, 8.90)
Beigi et al. [9], 2010	1	28	22	39	42.7	0.03 (0.00, 0.23)
Subtotal (95% CI)		**119**		**119**	**85.7**	**0.19 (0.09, 0.40)**
Total events	13		44			

Heterogeneity: $\chi^2 = 7.02$, d.f. = 5 ($p = 0.22$), $I^2 = 29\%$

Test for overall effect: $Z = 4.44$ ($p < 0.00001$)

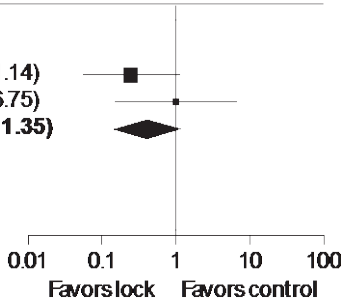


Incidence of relapse

Study or subgroup	Lock events	Lock total	Systemic antibiotics events	Systemic antibiotics total	Weight %	OR M-H, fixed (95% CI)
1.2.2 Lock + systemic antibiotics						
Rijnders et al. [15], 2005	3	21	9	23	45.9	0.26 (0.06, 1.14)
Fortun et al. [11], 2006	2	19	3	29	13.2	1.02 (0.15, 6.75)
Subtotal (95% CI)		**40**		**52**	**59.1**	**0.43 (0.14, 1.35)**
Total events	5		12			

Heterogeneity: $\chi^2 = 1.25$, d.f. = 1 ($p = 0.26$), $I^2 = 20\%$

Test for overall effect: $Z = 1.45$ ($p = 0.15$)



O'Horo JC, Am J Nephrol. 2011

PREFABL: predictors of failure of antibiotic locks for the treatment of catheter-related bacteraemia

Table 3. Model results: predictors of success/failure of CRB treatment with ABL solutions identified by PROC GLIMMIX multivariate analysis of data from 149 CRB in 61 chronic haemodialysis patients using long-term catheters as vascular access

Dependent variable	Variables in final model	Estimate	Standard error	Odds ratio	P-value	Covariance structure
'2-week outcome' (cleared)	CRB aetiology[a]	NA[a]	NA[a]	NA[a]	**0.033**	CSH
	CNS *vs Enterobacter/Acinetobacter*	1.24	0.67	3.44	0.067	
	CNS *vs Enterococcus* species	2.05	0.69	7.75	**0.004**	
	CNS *vs Klebsiella* species	0.46	0.87	1.59	0.596	
	CNS *vs Staphylococcus aureus*	1.38	0.68	3.97	**0.044**	
	CNS *vs Stenotrophomonas/Pseudomonas* species	2.04	0.88	7.74	**0.021**	
'6-week outcome' (clear)	Age (per 1-year increment)	0.14	0.07	1.15	**0.048**	CSH
	Phosphorous (per 1-mg/dL increment)	−0.40	0.12	0.67	**<0.001**	

Odds ratios for '2-week outcome' are odds of being cleared. Odds ratios for '6-week outcome' are odds of persisting clear.
[a]CRB aetiology is a categorical variable with six levels. A single parameter estimate is not applicable.
The bold values are the statistically significant P-values.

50 pediatric hemodialysis patients
149 CRB treated with systemic Abs + ABL
30 failed to be cleared
CRB aetiology was the only statistically significant independent variable for 2-week outcome (P = 0.033)

Onder AM, Nephrol Dial Transplant 2010

Treatment of Catheter infections

The catheter must be removed in case of

- Persistent fever 2-3 dys after systemic AB initiation
- Persistent bacteremia >3 dys after systemic AB initiation
- Bacteremia that is complicated by metastatic infection

Catheter salvage is always risky

Taking home messages

- Solutions verrous doivent suivre un processus de mise sur le marché en tout point semblable à celui des médicaments :
    Stabilité chimique, efficacité, toxicité
    Analyse du ratio risque / bénéfice et des coûts

- En traitement préventif
    Récidives de septicémies liées aux cathéters en dépit de pratiques de soins optimales
    Préférer les biocides aux antibiotiques

-En traitement curatif
    En association à l'AB systémique
    Patients stables, sans tunnellite
    Infections non liées à S aureus, P aeruginosa, candida ou BMR/BHR
    Retirer le cathéter à J3 du traitement si fièvre ou bactériémie persistante